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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,487	03/26/2001	Susanne Dagmar Pippig	4-31193A	9170

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EXAMINER
LI, RUIXIANG

ART UNIT	PAPER NUMBER
1646	20

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/817,487	PIPPIG ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11,12,14,17-20 and 25-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-9,11,12,14, and 17-20* is/are rejected.

7)☒ Claim(s) *5 and 25-28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Finality of Last Office Action

On further consideration, the finality of the rejection of the last Office action has been withdrawn by the Examiner because of a new ground of art rejection.

Amendment

The amendment filed in Paper No. 19 on June 12, 2003 has been entered. Claims 1-9, 11, 12, 14, 17-20, and 25-28 are pending and are under consideration.

Declaration/§119(e) Benefit Claim

Applicants are correct in that the claim to Provisional Application No. 60/266,331 is set forth in the first paragraph of the specification. The domestic priority does not need to be claimed in the declaration forms.

Withdrawn Objections and/or Rejections

The rejection of claims 1-4, 6-8, 11, and 12 under 35 U.S.C. §102 (a) as being anticipated by Zhou et al. (*J. Cell Biology* 146:1133-1146, September 6, 1999), as set forth at pages 5-6 of the previous Office Action (Paper No. 12, September 3, 2002), has been withdrawn in view of Applicant's Declaration under 37 C.F.R. §1.131.

The rejection of claims 9, 14, 17, 19, and 20, under 35 U.S.C. §103(a) as being unpatentable over Bordignon et al. (WO 95/06723, March 9, 1995) in view of Zhou et al. (*J. Cell Biology* 146:1133-1146, September 6, 1999), as set forth at pages 7-8 of the previous Office Action (Paper No. 12, September 3, 2002), has been withdrawn in view of Applicant's Declaration under 37 C.F.R. §1.131.

The objection of claims 5 and 25-28 set forth in the record has been withdrawn because the rejection of the base claim which claims 5 and 25-28 depend upon has been overcome for the reasons set forth above.

Claim Rejections Under 35 U. S. C. § 103 (a)

Claims 1-4, 6-9, 11, 12, 14, and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bordignon et al. (*IDS*, WO 95/06723, March 9, 1995) in view of Valenzuela et al. (WO 97/21811, June 19, 1997).

Bordignon et al. teach a method of marking a mammalian cell by expressing in this cell a nucleic acid, said nucleic acid encoding a cell surface receptor, and by subsequently presenting said receptor at the cell surface, characterized by using a nucleic acid in which the region encoding the intracellular domain of the receptor has been completely or partly deleted or modified in such a way that the receptor presented at the surface cannot, after binding to its binding partner, effect any signal transduction, is effective and usable in gene therapy (Abstract; claim 1-6).

Bordignon et al. also teach a method for the immunoselection of transfected cells, a method for the immunoseparation of transfected cells, and a method for the preparation and expansion of hematopoietic cells (see, e.g., claims 7-9; pages 4-7). Furthermore, Bordignon et al. teach identification of the genetically modified receptor with a marked antibody (1st paragraph to 2nd paragraph of page 4; claims 1-9); introduction of nucleic acid into mammalian cells (including hematopoietic cells) by means of a viral vector (see, e.g., claims 5, 9-11), preferably, a retrovirus vector (bottom of page 2) derived from Moloney murine leukemia virus (MoMLV; bottom of page 8).

Bordignon et al. clearly teach methods that comprise all the steps recited in the instant claims except the use of a cell surface mMuSK-R or MuSK-R as an identification marker for the genetically modified mammalian cells.

Valenzuela et al. teach a rat muscle specific tyrosine kinase receptor which shares 93.9% sequence identity with SEQ ID NO: 2 (Fig. 1; Example 1) and the nucleic acid sequence encoding the receptor (see attached sequence alignment). Valenzuela et al. also teach a protein or peptide that comprises the extracellular domain of MuSK-R, the nucleic acid which encodes such extracellular domain, and vectors comprising an isolated nucleic acid molecule encoding MuSK-R or its extracellular domains, which can be used to express MuSK-R in mammalian cells (bottom of page 8 to top of page 9). Specifically, Valenzuela et al. teach the extracellular domain of the mature protein (21-492), transmembrane domain (493-521), and intracellular domain (522-868) (bottom of page 19 to top of page 20; also see sequence alignment, Result 5). Valenzuela et al.

further teach a human muscle specific tyrosine kinase receptor which shares 99.8% sequence identity with SEQ ID NO: 2 and differs only by one conservative substitution of amino acid residue at position 433 (see attached sequence alignment) and the nucleic acid encoding the receptor protein (pages 19-21; Figure 4; Example 4). Deletion of the intracellular domain of MuSK-R (e.g., rat MuSK-R) would result in deletion of 347 amino acid residues. In addition, Valenzuela et al. teach an antibody which specifically binds the MuSK receptor (top of page 22). Finally, Valenzuela et al. teach that a MuSK-R is expressed in normal and denervated muscles, as well as other tissues including heart, spleen, ovary or retina (bottom of page 8).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to produce and use mMuSK-R in view of the teachings Bordignon et al. and Valenzuela et al. for identifying the genetically modified hematopoietic cells or for the immunoselection of transduced mammalian cells with a reasonable expectation of success. One would have been motivated to do so because (i) Bordignon et al. teach the use of a mutated cell surface receptor for identifying genetically modified mammalian cells including human hematopoietic cells (claim 11) or for immunoselection/immunoseparation of transduced mammalian cells. Such a mutated receptor with the intracellular domain either being partially or completely deleted cannot, after binding to its binding partner, effect any signal transduction, and thus is effective and usable in gene therapy (see, e.g., Abstract; pages 6-7); and (ii) Valenzuela et al. teach a cell surface MuSK-R and its extracellular domain, transmembrane domain, and intracellular domain, which can be used to make a

mMuSK-R. It would have also been obvious to one having ordinary skill in the art at the time the invention was made to use a MuSK-R as a masking marker with a reasonable expectation of success because expression of a MuSK-R in human hematopoietic cells would not be expected to effect any signal transduction and to interfere with the functions of the cells since a MuSK-R is not expressed in human hematopoietic cells, and thus it is effective and usable in gene therapy.

Claim Objections

Claims 5 and 25-28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday-Friday, 8:30 am-5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ruixiang Li
Examiner
July 10, 2003

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